28. The method of Claim 27 wherein said non-racemic mixture comprises at least 75% (+)(S) enantiomer of said carprofen.

29. The method of Claim 28 wherein said non-racemic mixture comprises at least 85% (+)(S) enantiomer of said carprofen.

30. The method of Claim 29 wherein said non-racemic mixture comprises at least 90%(+)(S) enantiomer of said carprofen.

31. The method of Claim 30 wherein said non-racemic mixture comprises at lest 95%(+)(S) enantiomer of said carprofen.

32. The method of Claim 31 wherein said non-racemic mixture comprises at least 99%(+)(S) enantiomer of said carprofen.

33. The method of Claim 32 wherein said non-racemic mixture is comprised almost entirely of (+)(S) enantiomer of carprofen.

34. A method of identifying a compound as an anti-inflammatory COX-2 inhibitor in dogs having a reduction in undesirable side effects associated with the simultaneous inhibition of COX-1, said method comprising:

evaluating the selectivity ratio of COX-2:COX-1 activity inhibition of said compound based on *ex vivo* inhibition levels in whole blood measured at a dose giving ≥ 80% COX-2 inhibition; and

identifying said compound as said anti-inflammatory COX-2 inhibitor when said selectivity ratio of COX-2:COX-1 is at least 3:1.

35. The method of Claim 34 wherein said selectivity ratio of COX-2:COX-1 activity inhibition at a dose giving ≥ 90% COX-2 inhibition.

36. The method Claim 34 further comprising prescribing said compound for use as an anti-inflammatory in dogs.

REMARKS

Via this submission, Claims 1, 4, 5, 8, 10, 11, 15-24 and 26 have been amended; Claims 2, 3, 6 and 7 have been cancelled; Claims 9, 12, 13 and 14 have been left intact; and Claims 27-36 have been added.

Claims 1, 4, 5, 8-36 now pend.

A Marked-Up Version of the Claims is attached for convenience.

The invention pertains to the alleviation of inflammation and pain in dogs. Several embodiments are being claimed in this regard:

a) Claims 1, 4, 5, 8-11 and 15-26: these are of record; they are directed to practices where treatment involves administration of compounds/drugs defined by Formula I. By way of amendment, these practices now expressly exclude 6-chloro-α-methyl-9H-carbazole-2-acetic acid, a.k.a. carprofen.

b) Claims 12, 13 and 14: these are of record; they are directed to a package suitable for use in commerce comprised of a suitable container and dosage form of the compound of Formula I, including carprofen, and printed instructional materials conveying certain information about the compound to the reader.

c) Claims 27-33: these are newly added; they are directed to practices where treatment involves a non-racemic mixture of carpofen.

d) Claims 34-36: these are newly added; they are directed to a method of identifying a compound as a COX-2 inhibitor in dogs, which compound has a coincident reduction in undesirable side effects otherwise associated with inhibition of the COX-1 isozyme.

Turning to the Official Action of December 31, 2001:

Claims 1-14:

Claims 5, 6, 8, 9 and 1, 2, 5, 6, 8 an 9 stand rejected under 35 USC 102, the citations being Berger et al (US 3896145) and either of the Holtsinger et al. or Vasseur et al. articles. Claims 3, 4, 7 and 10-14 are rejected under 35 USC 103 given any of the three preceding references. Reference is made to the June 5, 2001 Official Action for articulation of grounds.

Without acquiescing to the official reasons behind the maintenance of these rejections, Applicants have amended Claims 1, 4, 5, 8 10 and 11, and have cancelled without prejudice Claims 2, 3, 6 and 7. To wit: independent Claims 1 and 5 have been amended to claim those embodiments of the respective method and composition that employ other than carprofen as the drug or compound. Specifically, Applicants have added the language "with the proviso that said compound is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid." See e.g. In re Johnson, 194 USPQ 187 (CCPA 1977); Engineering Development Laboratories v.Radio Corporation of America, 68 USPQ 238 (CA2 1946). Consistently, Claims 2, 3, 6 and 7 have been cancelled. Conforming amendments have been made to Claims 4, 8, 10 and 11.

Applicants submit that the family of compounds remaining post amendment are neither disclosed nor suggested by Holtsinger et al. or Vasseur et al., each of which are directed to carprofen, in limited contexts. Other species of the genus claimed are not apparent, and have never been officially alleged to be so in this regard. Nor are the additional features of Claim 5, for example, found in or intimated by Berger, et al.

In regard to Claims 12, 13 and 14: these are directed to a package suitable for use in commerce. Reference to the previous Official Action in this case (June 5, 2001) subsumed herein freely admits that the art of record does not disclose the package claimed. Yet the claims are rejected on the allegation that modification of known pharmaceutical kits render them obvious. However, no art whatsoever is offered to substantiate this. It is unclear what "pharmceutical kits" are referred to, nor is it clear how and why one would be motivated to alter same to come to that which is claimed. Indeed, the official admission that the art of record does not disclose such a package contravenes the very existence of any such motivation.

It is further officially asseverated that the use of the (S) enantiomer --a feature of these particular claims-- would have been obvious inasmuch as racemic isomers are alleged to have differing properties. Again, no art is cited supportive of this contention. In point of fact, the record convincingly demonstrates that the (S) enantiomer is dramatically more functional than either the (R) isomer or the racemate, see Table 2: the COX-1/COX-2 Ratio for (R) enantiomer is given as ">4.19" with "129" for the racemate. The (S) enantiomer on the other hand exhibits a ratio of "181" which is approximately 40% higher than the racemic ratio ("129"). This magnitude of improvement for a specific enantiomer, let alone the (S) enantiomer, is wholly unexpected from the art of record, which art notably is not relied upon as a basis for this rejection in any event.

Withdrawal of the subject rejections is respectfully requested. If maintained, Applicants respectfully request identification of relevant art behind same and full elucidation of how it applies.

Claims 15-26:

These were added by Preliminary Amendment of June 11, 2001. Claim 15 is rejected under 35 USC 102 citing Holtsinger et al. or Vasseur et al. Claims 16-26 are rejected under 35 USC 103, Holtsinger et al. and Vasseur again in point, with Claims 24-25 further rejected under 103 on Berger et al.

Without concession, Applicants have amended Claims 15-24 and 26 to excise carprofen from the genus as done above, see Claims 15, 18, 21, 24 and 26 ("...with the proviso..."); the remaining claims are amended for conformation.

As indicated above, none of Holtsinger et al., Vasseur et al. nor Berger et al. describe or presage the sub-genus in the context now claimed, after amendment.

Withdrawal of the subject rejections is accordingly requested.

Claims 27-33:

These are added hereby. Support is at e.g. page 16 line 33 to page 17 line 12 of the specification. They are directed to methods of treatment using a non-racemic mixture of carprofen, e.g. the (S) enantiomer in various percentages. Such methods are not described or foreseen by the art of record. In particular, these references employ the racemic form of carprofen, again in limited use settings. Use of the non-racemate along with the unpredictable and significant increase in performance ascribed to same, including the (S) enantiomer, see discussion of Table 2 above, is not apparent from the art.

Favorable consideration and allowance of these claims is requested.

Claims 34-36:

These are newly added hereby. Support is at e.g. page 31 lines 8-23. They are directed to a method of identifying a compound as an anti-inflammatory COX-2 inhibitor and the prescribing of a compound that satisfies the criteria claimed. The art of record does not acknowledge, even obliquely, the parameters of these claims. Indeed, the Official Action admits that such are not found in same, e.g. the terms COX-2 or COX-1 are concededly not disclosed.

Favorable consideration and allowance of these claims is requested.

WHEREFORE it is believed that the instant case is in condition for allowance in its entirety, passage to which is respectfully requested.

Respectfully submitted,

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Registration No. 32,608

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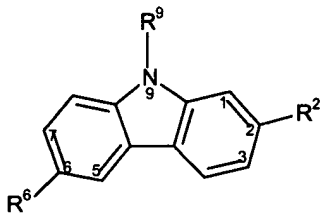
RLC:bk

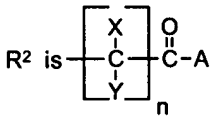
VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. **(Amended)** A method of treating or preventing pain and inflammatory processes and diseases associated with the activity of inducible cyclo-oxygenase-2 (COX-2) in a member of the species *Canis familiaris* in need of such treatment, while at the same time reducing or eliminating undesirable side effects associated with simultaneous inhibition of the activity of constitutive cyclo-oxygenase-1 (COX-1) by selectively inhibiting COX-2 activity with reference to COX-1 activity, wherein the selectivity ratio of COX-2:COX-1 activity inhibition is at least 3:1 based on *ex vivo* inhibition levels in whole blood measured at a dose giving ≥ 80% COX-2 inhibition, comprising administering to said member of the species *Canis familiaris* an amount therapeutically effective for treating pain and inflammation in accordance with the above-recited limitations, of an anti-inflammatory selective COX-2 inhibitory compound comprising a compound of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation**, with the proviso that said compound is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.

4. **(Twice Amended)** A method for treating or preventing inflammatory processes and diseases as in Claim**[s]** 1 **[,2 or 3]** further comprising wherein said inhibitory compound is used in combination with one or more other therapeutically active agents under the following conditions:

A. where a joint has become seriously inflamed as well as infected at the same time by bacteria, fungi, protozoa, and/or virus, said inhibitory compound is administered in combination with one or more antibiotic, antifungal, antiprotozoal, and/or antiviral therapeutic agents;

B. where a multi-fold treatment of pain and inflammation is desired, said inhibitory compound is administered in combination with inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting of:

1. NSAIDs;
2. H_1-receptor antagonists;
3. kinin-B_1 - and B_2 receptor antagonists;
4. prostaglandin inhibitors selected from the group consisting of PGD-, PGF-PGI_2 -, and PGE-receptor antagonists;
5. thromboxane A_2 (TXA2-) inhibitors;
6. 5- and 12-lipoxygenase inhibitors;
7. leukotriene LTC_4 - LTD_4/LTE_4- , and LTB_4 -inhibitors
8. PAF-receptor antagonists;
9. gold in the form of an aurothio group together with one or more hydrophilic groups;
10. immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine, and methotrexate;
11. anti-inflammatory glucocorticoids;
12. penicillamine;

13. hydroxychloroquine;

14. anti-gout agents including colchicines; xanthine oxidase inhibitors including allopurinol; and uricosuric agents selected from probeneoid, sulfinpyrazone, and benzobromarone;

C. where older dogs are being treated for disease conditions, syndromes, and symptoms found in geriatric dogs, said inhibitory compound is administered in combination with one or more member independently selected from the group consisting of:

1. cognitive therapeutics to counteract memory loss and impairment;

2. anti-hypertensives and other cardiovascular drugs intended to offset the consequences of atherosclerosis, hypertension, myocardial ischemia, angina, congestive heart failure, and myocardial infarction, selected from the group consisting of:

a. diuretics;

b. vasodilators;

c. ß-adrenergic receptor antagonists;

d. angiotensin-II converting enzyme inhibitors (ACE-inhibitors), alone or optionally together with neutral endopeptidase inhibitors;

e. angiotensin II receptor antagonists;

f. renin inhibitors;

g. calcium channel blockers;

h. sympatholytic agents;

i. α_2-adrenergic agonists;

j. α-adernergic receptor antagonists; and

k. HMG-CoA-reductase inhibitors (anti-hypercholester-olemics);

3. antineoplastic agents selected from:

a. antimitotic drugs selected from:

i. vinca alkalodis selected from:

[1] vinblastine, and

[2] vincristine;

4. growth hormone secretagogues;

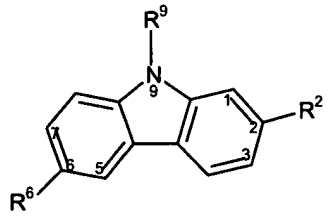
5. strong analgesics;

6. local and systemic anesthetics; and

7. H_2 -receptor antagonists, proton pump inhibitors, and other gastroprotective agents.

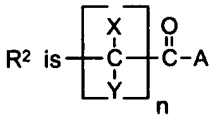
5. **(Amended)** A pharmaceutical composition for treating or preventing pain and inflammatory processes and diseases associated with the activity of inductible cyclo-oxygenase-2 (COX-2) in a member of the species *Canis familaris* in need of such treatment, while at the same time reducing or eliminating undesirable side effects associated with simultaneous inhibition of the activity of constitutive cyclo-oxygenase-1 (COX-1), comprising:

A. a therapeutically effective amount for treating pain and inflammation, of an anti-inflammatory selective COX-2 inhibitory compound which selectively inhibits COX-2 activity with reference to COX-1 activity, wherein the selectivity ration of COX-2; COX-1 activity inhibition is at least 3:1 based on *ex vivo* inhibition levels in whole blood measured at a dose giving ≥ 80% COX-2 inhibition, comprising an anti-inflammatory selective COX-2 inhibitory compound comprising a compound of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, **with the proviso that said compound is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid.**

10. (Amended) A pharmaceutical composition as in Claim 9 comprising an oral controlled release [carprofen] dosage form able to maintain plasma [carprofen] levels **of said pharmaceutical composition** above approximately 10 μg/mL for a period of time greater than 10.5 hours, when administered at a dose of about 2 mg/lb or less.

11. **(Twice Amended)** A pharmaceutical composition as in Claim**[s]** 5 **[,6 or 7]** further comprising said anti-inflammatory selective COX-2 inhibitory compound in combination with one or more other therapeutically active agents independently selected from the group consisting of:

A. anti-infectious agents comprising one or more antibiotic, antifungal, antiprotozoal, or antiviral therapeutic agents;

B. inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting of:

1. NSAIDs;

2. H_1-receptor antagonists;

3. kinin-B_1 - and B_2 receptor antagonists;

4. prostaglandin inhibitors selected from the group consisting of PGD-, PGF-PGI_2 -, and PGE-receptor antagonists;

5. thromboxane A_2 (TXA2-) inhibitors;

6. 5- and 12-lipoxygenase inhibitors;

7. leukotriene LTC_4 - LTD_4/LTE_4- , and LTB_4 -inhibitors

8. PAF-receptor antagonists;

9. gold in the form of an aurothio group together with one or more hydrophilic groups;

10. immunosuppressive agents selected from the group consisting of cyclosporine, azathioprine, and methotrexate;

11. anti-inflammatory glucocorticoids;

12. penicillamine;

13. hydroxychloroquine;

14. anti-gout agents including colchicines; xanthine oxidase inhibitors including allopurinol; and uricosuric agents selected from probeneoid, sulfinpyrazone, and benzobromarone;

C. where older dogs are being treated for disease conditions, syndromes, and symptoms found in geriatric dogs, said inhibitory compound is administered in combination with one or more member independently selected from the group consisting of:

1. cognitive therapeutics to counteract memory loss and impairment;

2. anti-hypertensives and other cardiovascular drugs intended to offset the consequences of atherosclerosis, hypertension, myocardial ischemia, angina, congestive heart failure, and myocardial infarction, selected from the group consisting of:

a. diuretics;

b. vasodilators;

c. ß-adrenergic receptor antagonists;

d. angiotensin-II converting enzyme inhibitors (ACE-inhibitors), alone or optionally together with neutral endopeptidase inhibitors;

e. angiotensin II receptor antagonists;

f. renin inhibitors;

g. calcium channel blockers;

h. sympatholytic agents;

i. α_2-adrenergic agonists;

j. α-adernergic receptor antagonists; and

k. HMG-CoA-reductase inhibitors (anti-hypercholester-olemics);

3. antineoplastic agents selected from:

a. antimitotic drugs selected from:

i. vinca alkalodis selected from:

[1] vinblastine, and

[2] vincristine;

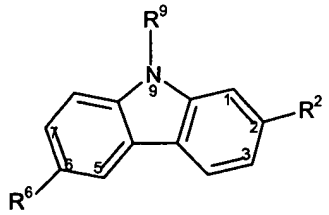
4. growth hormone secretagogues;

5. strong analgesics;

6. local and systemic anesthetics; and

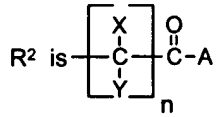
7. H_2 -receptor antagonists, proton pump inhibitors, and other gastroprotective agents.

15. (Amended) A method of preventing or alleviating pain and inflammatory processes and diseases in a member of the species Canis familiaris with reduced or no undesirable gastro-intestinal side effects normally associated with administration to said member of non-steroidal anti-inflammatory drugs, said member having been examined by a veterinarian practitioner and diagnosed as in need of such treatment using a drug which selectively inhibits inducible cyclo-oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes with substantially no inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce or avoid said side effects, which comprises administering to said member of the species Canis familiaris that has been so examined and diagnosed an amount therapeutically effective to treat or prevent pain and inflammation with reduction in or avoidance of said side effects of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

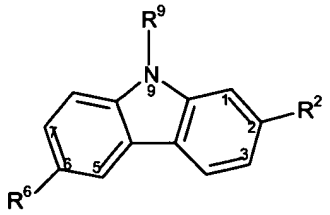
where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are

therapeutically active for treating or preventing pain and inflammation, **with the provis that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.

16. (Amended) The method according to claim 15 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily **by** oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of **[carprofen] said drug**.

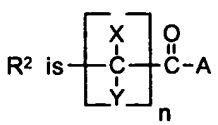
17. **(Amended)** The method according to claim 15 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily by injection containing from 25 to 100 mg of **[carprofen] said drug**.

18. **(Amended)** A method of treating a member of the species Canis familiaris, which member has been evaluated and determined to be (1) in need of treatment to alleviate or prevent pain and inflammatory processes and diseases with reduced or no undesirable gastro-intestinal side effects normally associated with administration of non-steroidal anti-inflammatory drugs to said member and (2) said member will benefit by using such treatment from the selective inhibition of inducible cyclo-oxygenase-2 (COX-2) to prevent or alleviate said pain and inflammatory processes with little or reduced inhibition of constitutive cyclo-oxygenase-1 (COX-1) to reduce or avoid said side effects, comprising administering to said member of the species Canis familiaris which has been so evaluated and diagnosed an amount therapeutically effective to treat or prevent pain and inflammation of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, **with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.

19. **(Amended)** The method according to claim 18 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily **by** oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of **[carprofen] said drug**.

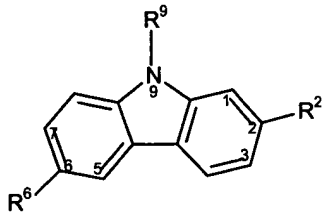
20. **(Amended)** The method according to claim 18 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily by injection containing from 25 to 100 mg of **[carprofen] said drug**.

21. **(Amended)** A method of treating a member of the species Canis familiaris to prevent or alleviate pain and inflammatory processes and diseases which comprises administering to a member of such species which has been

a) evaluated and determined by a veterinarian practitioner to be in need of such treatment with a drug which inhibits the activity of inducible cyclo-oxygenase-2(COX-2) to prevent or alleviate said pain and inflammatory processes while

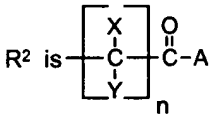
(b) avoiding or reducing the gastro-intestinal side effects normally associated with administration of non-steroidal anti-inflammatory drugs to said member and therefore

(c) to benefit from treatment with a drug that does not substantially inhibit the activity of constitutive cyclo-oxygenase-1(COX-1) so that said side effects are reduced or eliminated, which method comprises administering to said member of the species Canis familiaris which has been so evaluated and determined, a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation,

whereby such pain and inflammation are prevented or alleviated, said side effects are avoided or reduced and COX-2 is selectively inhibited without substantial inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least 3:1 based on ex vivo inhibition levels measured in whole blood**, with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.

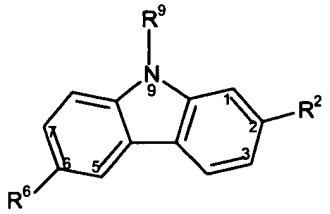
22. **(Amended)** The method according to claim 21 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily **by** oral administration of a caplet, chewable tablet, or suspension containing from 25 to 100 mg of **[carprofen]** **said drug**.

23. **(Amended)** The method according to claim 21 where the pain and inflammation is caused by osteoarthritis, **[the drug administered is carprofen]** and administration is once or twice daily by injection containing from 25 to 100 mg of **[carprofen]** **said drug**.

24. **(Amended)** A pharmaceutical combination for treating or preventing pain and inflammatory processes and diseases associated with the activity of inducible cyclo-oxygenase-2 (COX-2) in a member of the species Canis familaris with reduced or no side effects normally associated with the inhibition of the activity of constitutive cyclo-oxygenase -1 (COX-1) comprising

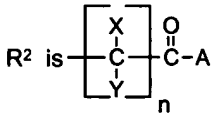
(1) a pharmaceutical composition comprising

(a) a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;
R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation, and

(b) a pharmaceutically acceptable carrier therefor, in association with

(2) printed informational material conveying that said pharmaceutical composition contains a therapeutic agent, which when administered to said member effectively inhibits the activity of COX-2 to prevent said pain and inflammatory processes and diseases while reducing or eliminating undesirable gastro-intestinal side effects by substantially avoiding inhibition of the activity of COX-1, **with the proviso that said pharmaceutical composition is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.

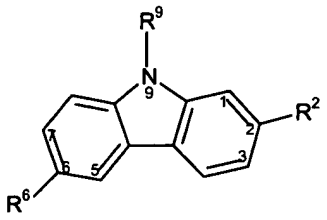
26. **(Amended)** A method of treating a member of the species Canis familiaris to prevent or alleviate pain and inflammatory processes and diseases which comprises

(a) evaluating said member by a veterinarian practitioner to determine if the member is in need of treatment with a drug which inhibits the activity of inducible cyclo-oxygenase-2 (COX-2),

(b) evaluating said member by a veterinarian practitioner to determine if the member would benefit from the treatment with a drug that does not substantially inhibit the activity of constitutive cyclo-oxygenase-1 (COX-1) so that gastro-intestinal side effects will be reduced or avoided,

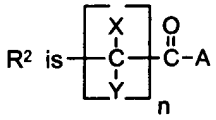
(c) determining that said member will be benefited from the treatment with a drug that selectively inhibits the activity of COX-2 with little or no inhibition of the activity of COX-1, and

(d) administering to said member of the species Canis familiaris which has been so evaluated and determined, a therapeutically effective amount of the formula:



Formula (I)

wherein:



where A is hydroxy, (C_1 - C_4)alkoxy, amino, hydroxyamino, mono-(C_1 - C_2)alkylamino, di-(C_1 - C_2)alkylamino; X and Y are independently H or (C_1 - C_2)alkyl; and n is 1 or 2;

R^6 is halogen, (C_1 - C_3)alkyl, trifluoromethyl, or nitro;

R^9 is H; (C_1 - C_2)alkyl; phenyl or phenyl-(C_1 - C_2)alkyl, where phenyl is optionally mono-substituted by fluoro or chloro; -C(=O)-R, where R is (C_1 - C_2)alkyl or phenyl, optionally mono-substituted by fluoro or chloro; or -C(=O)-O-R^1 , where R^1 is (C_1 - C_2)alkyl;

where X and Y are different, the (-)(*R*) and (+)(*S*) enantiomers thereof; and all pharmaceutically acceptable salt forms, prodrugs and metabolites thereof which are therapeutically active for treating or preventing pain and inflammation,

whereby such pain and inflammation are prevented or alleviated, said side effects are avoided or reduced and COX-2 is selectively inhibited without substantial inhibition of COX-1, the selective inhibition ratio of COX-2 to COX-1 being at least 3:1 based on ex vivo inhibition levels measured in whole blood, **with the proviso that said drug is not 6-chloro-α-methyl-9H-carbazole-2-acetic acid**.